tion, as well as on lung cell damage (measured by lavage fluid LDH activity and total protein), were evaluated. In the absence of any histopathological changes, lung cell damage, or pulmonary inflammation, a single inhalation of PM10 at 200 $\mu g/m^3$ significantly depressed superoxide ($O_2^{\cdot -}$) production by pulmonary Mø, and increased and decreased the number of circulating neutrophils and lymphocytes, respectively, in the blood 3 hr following exposure; after 24 hr, lavaged cell numbers were elevated, but production of $O_2^{\cdot -}$ and blood cell numbers were similar to that of air (unconcentrated NYC air) controls. Blood cell values were also significantly altered at the lower exposure concentration after 3 hr. These studies begin to provide a mechanism which may underlie the observed epidemiological evidence. Supported by Health Effects Institute Contract #94-03A.

394 *IN VIVO* EVIDENCE OF FREE RADICAL GENERATION IN THE LUNG TISSUE OF RATS AFTER EXPOSURE TO AN AIR POLLUTION PARTICLE.

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The environmental impact on the presence of air pollution particle, oil fly ash (OFA), has become an increasingly serious health hazard. Although studies in chemical and biological systems have demonstrated that OFA is cytotoxic, no evidence for the generation of free radicals *in vivo* has been provided. We have employed an ESR spin trapping technique to detect an adduct of the spin trap α-(4-pyridyl-1-oxide)-*N-tert* butyl nitrone (POBN) in the lipid extract of lung tissue from rats 24 hours after exposure to OFA. We studied also free radical generation after exposure to both the insoluble and soluble fraction of the air pollution particle. The ESR spectrum of the radical adduct present in the lipid extracts of lung tissue exhibited hyperfine coupling constants α^N = 15.0G and α^H_β = 2.5G for the OFA and the soluble fraction of the air pollution particle. The radical adducts detected from both fractions are proposed to be lipid derived free radicals generated in the lungs of treated rats. The insoluble fraction of the air pollution particle gave ESR signals not significantly different from that of the controls. This is the first report which employs ESR to demonstrate free radical generation *in vivo* due to air pollution particle.

395 PULMONARY RESPONSES OF RATS TO INTRATRACHEAL INSTILLATION OF DIESEL EXHAUST PARTICLES: INFLAMMATION, OXIDATIVE STRESS AND ALVEOLAR MACROPHAGE CYTOKINE SECRETION.

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The objective of this study was to investigate the acute pulmonary responses of rats to diesel exhaust particles (DEP). Male Sprague-Dawley rats were dosed intratracheally with DEP (5 and 35 mg/kg body weight) or saline vehicle and killed 1, 3 and 7 days after the instillation. The pulmonary responses were evaluated by analysis of indicators of pulmonary inflammation, oxidative stress and injury in bronchoalveolar lavage (BAL) fluid, measurement of oxygen consumed by BAL cells, and analysis of the ability of alveolar macrophages (AM) to release interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-α). DEP instillation resulted in dose- and time-related pulmonary inflammation and injury, as evidenced by an increased infiltration of neutrophils and elevated levels of total proteins, albumin, lactate dehydrogenase and β-galactosidase in BAL fluid. There were increased BAL cell oxygen consumption, phospholipidosis and elevated antioxidant enzyme activity observed in DEP-treated rats, indicating oxidative stress had occurred in these rats. DEP exposure resulted in transient secretion of TNF-α and persistent secretion of IL-1 by AM. The secretion of these cytokines by AM obtained from DEP-exposed rats following *in vitro* LPS stimulation was significantly depressed. In summary, DEP caused oxidative stress, that may be responsible for activating AM and leading to initiation and modulation of DEP-induced pulmonary inflammation and injury. IL-1 seems a more prominent contributor than TNF-α in this process. The suppression of the AM response to LPS after DEP exposure supports the concept that exposure to DEP may compromise the host defense system.

396 PULMONARY INFLAMMATION AFTER COMBINED EXPOSURES TO LIPOPOLYSACCHARIDE (LPS) AND AN HERBICIDE, PROPANIL.

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Propanil (PRO) is applied extensively by aerosol to wheat and rice. PRO has been shown to markedly alter LPS-induced macrophage cytokine secretion. Since inhalation exposure to LPS is common in agriculture and causes lung inflammation through macrophage cytokine secretion, we queried whether combined exposures to PRO and LPS might affect these inflammatory responses. PRO (400 mg/kg) dissolved in peanut oil (PO) or PO alone were administered by gavage to C57BL/6 mice. 3 days later, PRO- and PO-treated mice underwent intratracheal (IT) instillation of saline, 0.1 μg LPS, or 1.0 μg LPS. 1 day later, mice underwent bronchoalveolar lavage (BAL) with measurement of BAL total protein, total cells, and differential cell counts. Relative to IT saline, IT LPS induced increases in BAL total cells, neutrophils, and total protein. No differences were noted between PRO and PO groups after either IT saline or LPS. These studies do not support an important role for PRO in modifying pulmonary inflammatory responses to LPS.

397 NITRIC OXIDE-INDUCED PROSTAGLANDIN RELEASE BY RAT ALVEOLAR MACROPHAGES.

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There is a growing body of evidence demonstrating links between the nitric oxide synthase and cyclooxygenase pathways. We hypothesized that nitric oxide (NO) might increase the release of prostaglandins (PG) by alveolar macrophages (AM). AM were obtained from male Sprague-Dawley rats by bronchoalveolar lavage and were cultured for 6 hours ± spermine-NO, a NO-liberating compound. Some cultures also contained superoxide dismutase (SOD). At the end of the culture period, cell supernatants were collected and assayed for NO products (Greiss method) and PGE_2 (enzyme-linked immunoassay). The spermine-NO complex increased NO products in the culture medium by 19-fold (22.5 vs. 424 μM). Such elevated NO levels increased PGE_2 release from AM 7-fold (73.3 vs. 545 pg/ml). SOD increased NO products in some cultures and had no effect in other cultures; in all cultures SOD increased PGE_2 release an average of 4-fold (73.3 vs 314 pg/ml). The combination of spermine-NO and SOD elevated PGE_2 (770 pg/ml). This effect of SOD on NO-induced PGE_2 release appeared to be additive, not synergistic. These results demonstrate that NO increases the release of PGE_2 from AM. Induction of NO production has been associated with in vivo exposure to various particulates. Since PG have been shown to decrease fibroblast proliferation, NO-enhanced PGE_2 release could represent a controlling or counterbalancing mechanism which may limit particle-induced fibrogenesis.

398 *IN VITRO* ARSINE METABOLISM AND DISTRIBUTION IN HUMAN ERYTHROCYTES.

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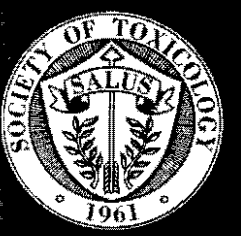
Arsine (AsH_3) is used in the electronics industry and can be generated accidentally from other arsenic (As) compounds. The mechanism by which AsH_3 causes hemolysis in erythrocytes (RBCs) appears to be mediated by a reaction between AsH_3 and oxyhemoglobin. The products of AsH_3 which are formed after this reaction are unknown; therefore, we determined the metabolism and distribution of AsH_3 among the cellular components of RBCs — protein, membrane, and cytosol. Metabolism in RBCs incubated at 37°C with 1mM AsH_3 was determined using a chloroform:methanol (2:1) extraction followed by analysis for total As. The distribution of As was ~82% bound to protein, ~16% in the aqueous phase and ~2% in the organic phase; this remained unchanged when measured in intervals of 15 min for up to 60 min. Characterization of the target protein and of the arsenic species bound to that protein will facilitate understanding of arsine's mechanism of toxicity. As species extracted into the aqueous phase were further characterized by ion-exchange chromatography. Trivalent As (As^{+3}) represented approximately 80% of the As in the aqueous phase and pentavalent As (As^{+5}) approximately 20%. Experiments using blood preincubated with a sulfur suspension resulted in unaltered distributions and metabolism; however, hemolysis induced by both 0.5mM and 1mM AsH_3 was reduced. These data indicate that the metabolic products measured here may not be sensitive to AsH_3-induced hemolysis. (Funded by NIH Grant ES6644).



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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster / discussion, workshops, roundtables, and poster sessions of the 36th Annual Meeting of the Society of Toxicology, held at the Cincinnati Convention Center, Cincinnati, Ohio, March 9-13, 1997.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 371.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 395.

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